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10/577,827	03/26/2007	Kazumi Koga	BY0033P	9797
210	7590	05/01/2008	EXAMINER	
MERCK AND CO., INC			LANDSMAN, ROBERT S	
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RAHWAY, NJ 07065-0907			PAPER NUMBER	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/577,827	<b>Applicant(s)</b> KOGA ET AL.	
	<b>Examiner</b> ROBERT LANDSMAN	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 2-6, 8 and 9 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 2 is/are allowed.
- 6) ☒ Claim(s) 3, 8 and 9 is/are rejected.
- 7) ☒ Claim(s) 4-6 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 May 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/29/07</u> . | 6) <input type="checkbox"/> Other: ____.  |

## **DETAILED ACTION**

### ***1. Formal Matters***

- A. Claims 1-9 are pending in the application and are the subject of this Office Action.

### ***2. Information Disclosure Statement***

- A. 37 CFR 1.98(b)(5) states -

Each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication.

Therefore, the references in the 1449 filed 10/29/07 have been considered, but will not be printed on the face of the patent.

### ***3. Specification***

When a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and a sequence identifier ("SEQ ID NO:X") must be used either in the drawing or in the Brief Description of the Drawings. See MPEP ' 2422.02. In the instant application, a sequence identifier must be used for the sequences appearing in Figure 1.

Appropriate correction is required.

### ***4. Claim Objections***

- A. Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 1 and 5 both ultimately recite the same nucleic acid since both claims recite "consisting of SEQ ID NO:1."

- B. Claims 4-6 are objected to since they depend from canceled claim 1.

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C. Claim 9 is objected to since it would be clearer if parts (a), (b) and (c) were further labeled as “(a)(1),” “(a)(2),” “(b)(1),” etc.

***5. Claim Rejections - 35 USC § 112, first paragraph - scope of enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 2 and 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while then being enabling for the protein of SEQ ID NO:2 and the nucleic acid of SEQ ID NO:1, does not reasonably provide enablement for nucleic acids which hybridize to SEQ ID NO:1, or for any isolated protein consisting of SEQ ID NO:2 with a substitution, deletion, addition, or insertion and having ORL1 activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming all nucleic acids which **hybridize** under stringent conditions to SEQ ID NO:1. Nucleic acid molecules which hybridize to SEQ ID NO:1 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to the polynucleotide of SEQ ID NO:1 and would **encode proteins with one or more** substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:2. Claim 8 recites similar protein limitations.

Applicants provide no guidance or working examples of nucleic acid molecules which hybridize to SEQ ID NO:1, or of proteins which with one or more substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:2 and have the recited “ORL1 activity.” Furthermore, Applicants do not provide a *function* of these nucleic acid molecules, or of the proteins which they encode, other than that they have “ORL1 activity.” Respectfully, “binding to an antigen” could be considered an ORL1 activity.

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Applicants have provided no guidance as to what critical residues are required to maintain the functional characteristics of the protein of SEQ ID NO:2. Furthermore, it is not predictable to one of ordinary skill in the art how to make a functional protein which is less than 100% identical to that of SEQ ID NO:2.

Furthermore, the scope of claim 9 is excessive with regard to Applicants claiming a method of screening **any and all ORL1 proteins**. The term “ORL1” is an acronym. Applicants have only taught screening the protein of SEQ ID NO:2. The specification has not disclosed how to screen all opioid “like” receptors. No guidance or working examples of opioid “like” proteins have been disclosed in the specification, nor is it predictable what the genus of proteins is which are “like” opioid receptors other than opioid receptors, especially in absence of a specific activity (e.g. binding nociceptin).

In addition, claim 9(c) recites a method which reads on **in vivo screening**. However, there is no guidance or working examples of such an assay

In summary, the breadth of the claims is excessive with regard to Applicants claiming all nucleic acids which hybridize to SEQ ID NO:1 and with regard to proteins with one or more substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:2. The same is true for the genus of proteins to be screened in claim 9. There is also a lack of guidance and working examples of these nucleic acid molecules and proteins as well as which residues are critical for protein function. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make a functional protein other than that of SEQ ID NO:2 leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

#### ***6. Claim Rejections - 35 USC § 112, first paragraph – written description***

A. Claims 2 and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Nucleic acid molecules which **hybridize** to SEQ ID NO:1 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said polynucleotides and would encode **proteins which have one or more** amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:2.

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The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1, or molecules which hybridize to this nucleic acid, along with the protein of SEQ ID NO:2, alone, are insufficient to describe the genus.

Furthermore, adequate written description is lacking with regard to Applicants claiming a method of screening **any and all ORL1 proteins**. The term “ORL1” is an acronym. Applicants have only taught screening the protein of SEQ ID NO:2. The specification has not disclosed how to screen all opioid “like” receptors. No description of opioid “like” proteins have been disclosed in the specification, nor does the specification describe the genus of proteins which is “like” opioid receptors other than opioid receptors, especially in absence of a specific activity (e.g. binding nociceptin).

In addition, claim 9(c) recites a method which reads on **in vivo screening**. However, no such assay is described in the specification.

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

#### ***7. Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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A. Claims 3, 5, 8 and 9 recite "ORL1." This term is an acronym and should be spelled out upon first use.

B. Claims 3, 8 and 9 are rejected since the metes and bounds of "ORL1 activity" are unknown. In other words, it is unclear as to what "activity" is being referred.

C. Claim 8 is confusing since it recites the transitional phrase, "consisting of," as well as the protein having an "addition," or "insertion." It is unclear how a protein consisting of SEQ ID NO:2, which is "closed" language, can also have an "insertion," or "deletion."

### 8. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 3, 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Evans et al. (US 6,432,652). The claims recite an isolated nucleic acid which hybridizes to SEQ ID NO:1 and which encodes a protein having ORL1 activity. The claims also recite a variant of SEQ ID NO:2 as well as methods of screening compounds for ORL1 activity. Evans teach a nucleic acid encoding an opioid receptor which is 93.5% identical to SEQ ID NO:1 of the instant invention (see Sequence Comparison A below). This nucleic acid has 96% similarity with SEQ ID NO:1. Therefore, it would be expected to hybridize to SEQ ID NO:1 even under the most stringent conditions.

The protein of Evans is 98.8% identical to SEQ ID NO:2 of the instant invention (see Sequence Comparison B below). There is, *inter alia*, a substitution at position 43.

Evans also teach the screening methods recited in claim 9 (column 6, lines 24-26 and Example 2).

### SEQUENCE COMPARISON A

```
US-08-405-271A-18
; Sequence 18, Application US/08405271A
; Patent No. 6432652
; GENERAL INFORMATION:
; APPLICANT: EVANS, CHRISTOPHER J.
; APPLICANT: KEITH, DUANE E.
; TITLE OF INVENTION: OPIOID RECEPTOR GENES
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```
;  NUMBER OF SEQUENCES:  25
;  CORRESPONDENCE ADDRESS:
;    ADDRESSEE:  MORRISON & FOERSTER
;    STREET:  2000 PENNSYLVANIA AVENUE, NW, Suite 5500
;    CITY:  WASHINGTON
;    STATE:  DC
;    COUNTRY:  USA
;    ZIP:  20006-1888
;  COMPUTER READABLE FORM:
;    MEDIUM TYPE:  Floppy disk
;    COMPUTER:  IBM PC compatible
;    OPERATING SYSTEM:  PC-DOS/MS-DOS
;    SOFTWARE:  PatentIn Release #1.0, Version #1.30
;  CURRENT APPLICATION DATA:
;    APPLICATION NUMBER:  US/08/405,271A
;    FILING DATE:  14-MAR-1995
;    CLASSIFICATION:  435
;  ATTORNEY/AGENT INFORMATION:
;    NAME:  MURASHIGE, KATE H.
;    REGISTRATION NUMBER:  29,959
;    REFERENCE/DOCKET NUMBER:  22000-20526.22
;  TELECOMMUNICATION INFORMATION:
;    TELEPHONE:  (202) 887-1500
;    TELEFAX:  (202) 887-0763
;    TELEX:  90-4030 MRSNFOERSWSH
;  INFORMATION FOR SEQ ID NO:  18:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  1805 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  double
;      TOPOLOGY:  linear
;    FEATURE:
;      NAME/KEY:  CDS
;      LOCATION:  10..1119
US-08-405-271A-18
```

```
Query Match          93.5%;  Score 1041;  DB 3;  Length 1805;
Best Local Similarity 96.0%;  Pred. No. 5.1e-193;
Matches 1068;  Conservative  0;  Mismatches  45;  Indels  0;  Gaps  0;
```

```
Qy      1  ATGGAGCCTCTCTTCCCCGCCCCATTCTGGGAGGTTATCTACGGCAGCCACCTTCAGGGC  60
        |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db      10  ATGGAGCCCCTCTTCCCCGCGCGGTTCTGGGAGGTTATCTACGGCAGCCACCTTCAGGGC  69

Qy      61  AACCTGTCCCTCCTCAGTCCCAACCACAGTCTGCTGCCTCCGCATCTGCTGCTCAATGCC  120
        |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db      70  AACCTGTCCCTCCTGAGCCCCAACCACAGTCTGCTGCCCCCGCATCTGCTGCTCAATGCC  129

Qy     121  AGTCACAGCGCCTTCCTGCCCTCGGGCTCAAGGTCACCATCGTGGGGCTCTACCTGGCC  180
        ||  |||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db     130  AGCCACGGCGCCTTCCTGCCCTCGGGCTCAAGGTCACCATCGTGGGGCTCTACCTGGCC  189

Qy     181  GTGTGTGTGCGGGGGCTCCTGGGGAAGTGCCTCGTCATGTACGTCATCCTCAGGCACACC  240
        |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db     190  GTGTGTGTGCGGAGGGCTCCTGGGGAAGTGCCTTGTCATGTACGTCATCCTCAGGCACACC  249

Qy     241  AAAATGAAGACAGCCACCAATATTTACATCTTTAACCTGGCCCTGGCAGACACTCTGGTC  300
        |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db     250  AAAATGAAGACAGCCACCAATATTTACATCTTTAACCTGGCCCTGGCCGACACTCTGGTC  309
```





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**SEQUENCE COMPARISON B**

ID ABG33031 standard; protein; 370 AA.  
 XX  
 AC ABG33031;  
 XX  
 DT 15-JUN-2007 (revised)  
 DT 19-NOV-2002 (first entry)  
 XX  
 DE Human opioid receptor ORL-1.  
 XX  
 OS Homo sapiens.  
 XX  
 PN US6432652-B1.  
 XX  
 PD 13-AUG-2002.  
 XX  
 PF 14-MAR-1995; 95US-00405271.  
 XX  
 PA (REGC ) UNIV CALIFORNIA.  
 XX  
 PI Evans CJ, Keith DE, Edwards RH, Kaufman D;  
 XX  
 DR WPI; 2002-681194/73.  
 DR N-PSDB; ABS53446.  
 DR PC:NCBI; gi4505513.  
 DR PC:SWISSPROT; P41146.  
 DR PC:BIND; 177237.  
 CC  
 CC Revised record issued on 15-JUN-2007 : Enhanced with precomputed  
 CC information from BOND.  
 XX  
 SQ Sequence 370 AA;

Query Match 98.8%; Score 1884; DB 5; Length 370;  
 Best Local Similarity 98.1%; Pred. No. 8.1e-200;  
 Matches 363; Conservative 3; Mismatches 4; Indels 0; Gaps 0;

Qy 1 MEPLFPAPFWEVIYGSHLQGNLSLLSPNHSLLPPHLLLNASHSAFLPLGLKVTIVGLYLA 60  
 |||  
 Db 1 MEPLFPAPFWEVIYGSHLQGNLSLLSPNHSLLPPHLLLNASHGAFLPLGLKVTIVGLYLA 60  
 |||  
 Qy 61 VCVGGLLGNCCLVMYVILRHTKMKTATNIYIFNLALADTLVLLTLFPQGTDILLGFWPFNG 120  
 |||  
 Db 61 VCVGGLLGNCCLVMYVILRHTKMKTATNIYIFNLALADTLVLLTLFPQGTDILLGFWPFNG 120  
 |||  
 Qy 121 ALCKTVIAIDYNNMFTSTFTLTAMSVDYVAICHPIRALDVRTSSKAQAVNVAIWALASV 180  
 |||  
 Db 121 ALCKTVIAIDYNNMFTSTFTLTAMSVDYVAICHPIRALDVRTSSKAQAVNVAIWALASV 180  
 |||  
 Qy 181 VGVFVAIMGSAQVEDEEIECLVEIPAPQDYWGPFVAVCFIFLFSFIVPVLIIISVCYSLMIR 240  
 |||:|||||  
 Db 181 VGVFVAIMGSAQVEDEEIECLVEIPTQDYWGPFVFAICIFLFSFIVPVLVISVCYSLMIR 240  
 |||  
 Qy 241 RLRGVRLLSGSREKDRNLRRITRLVLVVVAVFVGCWTPVQVFLVQGLGVQPGSETAVAI 300  
 |||  
 Db 241 RLRGVRLLSGSREKDRNLRRITRLVLVVVAVFVGCWTPVQVFLVQGLGVQPSSETAVAI 300  
 |||

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```

Qy      301 LRFCTALGYVNSCLNPILYAFLDENFKACFRKFCCASALRREVQVSDRVRSIKDVVALAC 360
          ||||||||||||||||||||||||||||||||||||||||:||||||||||||||||||
Db      301 LRFCTALGYVNSCLNPILYAFLDENFKACFRKFCCASALRRDVQVSDRVRSIKDVVALAC 360

Qy      361 KTSETVPRPA 370
          |||||||||||
Db      361 KTSETVPRPA 370

```

### 9. Conclusion

A. Claim 2 is allowable. Claims 4-6 are objected to as depending from a canceled claim.

### *Advisory information*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman, Ph.D. whose telephone number is (571) 272-0888. The examiner can normally be reached on M-F 10 AM – 6:30 PM (eastern).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Robert Landsman/  
Primary Examiner, Art Unit 1647